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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,427	05/10/2005	Hans-Georg Capraro	ON/4-32759A	5061
75/074	75/90	08/18/2008		
NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC. 400 TECHNOLOGY SQUARE CAMBRIDGE, MA 02139				
EXAMINER				
MOORE, SUSANNA				
ART UNIT		PAPER NUMBER		
1624				
MAIL DATE		DELIVERY MODE		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/534,427

Applicant(s)

CAPRARO ET AL.

Examiner

SUSANNA MOORE

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 May 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/CDC)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date _____

DETAILED ACTION

Response to Arguments

Applicant's argument, see Remarks, filed 5/14/2008, with respect to Office Action mailed 11/14/2007 have been fully considered. Some of the rejections have been withdrawn, others have been maintained. Thus, this is a Final Office Action. In summary, claims 1-7 and 9 are currently pending and under consideration.

Claim Objections

The objection of claim 8 for being of improper dependent form is withdrawn based on the cancellation of said claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection of claim 1, for the terms "unsubstituted or substituted" is withdrawn based on the amendment to said claim. On pages 3-5 of the Specification, there is a discussion of the concept of substitution. However, this passage fails to list the intended substituents. A number of examples are given using open terms. What other substituents is Applicant claiming? Where

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applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999).

Applicant states, "In response thereto, Applicants note that it is unclear whether the Examiner finds the terms unsubstituted or substituted unclear, or whether the Examiner understands the terms, but finds the claim indefinite because it is unclear what the possible substitutions are." In response to Applicant's remarks, the metes and bounds of substituted cannot be ascertained based on the claim language and the guidance provided in the Specification. Thus, the rejection is maintained.

The rejection of claim 1 under 35 U.S.C. 112, second paragraph, as being indefinite for R² as "a heterocyclic radical" is withdrawn based on the amendments.

Claims 1-6 and 9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In evaluating the enablement question, several factors are to be considered. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988); *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The

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nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples,

HOW TO MAKE: The nature of the invention in the instant case, has claims, which embrace a wide range of chemically and physically distinct compounds, wherein $X-R^4$ are a variety of variables with working examples only to $X = \text{oxygen}$ and $R^4 = \text{benzyl}$. The exact nature of these substituents are vague and indefinite in that it is not clear exactly how to make the compounds of the instant invention where there is more than the above-mentioned substituents on the phenyl ring. While many specific examples are disclosed, there is insufficient guidance for preparing the compounds where $X-R^4$ are not O-benzyl.

Patent Protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. *Genentech Inc. v. Novo Nordisk* 42 USPQ2d 1001.

Applicant traverses the above rejection by stating, "Compliance with the enablement requirement however, does not turn on whether an example is disclosed. The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. See MPEP 2164.02. In the present case, X is disclosed as being O, NH, and S, while R^4 is disclosed as a carbon linked R^7 group, R^7 being one of cyclobutyl, cyclopentyl, cyclohexyl, phenyl, furyl, pyrrolyl, thienyl or pyridyl. Given the disclosed experimental procedure showing the synthesis of O-benzyl compounds, one of skill in the art could certainly make amino and sulphur linked R^7 groups as disclosed above." Applicant is correct, the enablement requirement is not does not

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turn on whether and example is disclosed. However, this is one factor considered under the Wands analysis.

Furthermore, the availability of the starting material that is needed to prepare the invention as claimed is at issue here...As per MPEP 2164.01 (b). A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court in *In re Giron*, 442 F.2d 985, 991, 169 USPQ 723, 727 (CCPA 1971), made it clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. *In re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981). Thus, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirst et. al. (U.S. 6,713,474).

The instant invention claims compounds of formula (I), wherein R^1 = hydrogen, R^2 = 4-methylpiperazinyl, X = oxygen and R^4 = benzyl and X- R^4 is at the 3 position of the phenyl ring.

The reference teaches a compound of formula (I), wherein R^1 = hydrogen, R^2 = 4-methylpiperazinyl, X = oxygen and R^4 = benzyl. See column 130, lines 53-55. Another species found in the reference is a compound of formula (I), wherein R^1 = hydrogen, R^2 = 4-methylpiperazinyl, X = oxygen and R^4 = benzyl and X- R^4 is at the 4 position of the phenyl ring.. See column 130, lines 53-55.

The difference between the claimed compound and the reference is the position of the X- R^4 on the phenyl ring, the 4 position versus Applicant's 3 position. The MPEP 2144.09 states "Compounds which are position isomers (compounds having the same radicals in physically

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different positions on the same nucleus)... are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).

Moreover, the generic structure of Hirst encompasses the instantly claimed compounds (see Formula I, column 9) as claimed herein. Columns-9-12, define the substituents as follows: R¹ is hydrogen, substituted or unsubstituted aliphatic group, halogen; R² is substituted or unsubstituted cycloalkyl group, etc.; X= O, NH, S; and R⁴ is substituted or unsubstituted aralkyl group, substituted or unsubstituted heteroaralkyl group, etc. The compounds of the instant invention are generically embraced by Hirst in view of the interchangeability of the substitutions of the pyrrolo[2,3-d]pyrimidine. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example NHCH₂phenyl for X-R⁴ as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

The same arguments applied above can be directed towards the following references: U.S. 2003175935, 2003082622, 2003153752; WO 2001072751 and 2000017202. These references have the same specie listed above in the art rejection. The references also teach genus equivalency teachings of the substituents.

Applicant traverses the above rejection by stating, "In applying the test for obviousness to chemically similar structures, the Court of Appeals Federal Circuit recently laid out a standard in *Takeda Chemical Industries Ltd v. Alphabarm Pty. Ltd.* 83 USPQ2d 1169 (Fed. Cir. 2007). The Court stated, "in many cases involving new chemical compounds, it remains necessary to

identify some reason that would have led a chemist to modify a known compound in a particular manner to establish a prima facie case of obviousness in order to find a prima facie case of obviousness (for structurally related compounds), a showing that the 'prior art would have suggested making the molecular modifications necessary to achieve the claimed invention' was also required."

In the present case, Hirst broadly discloses close to 600 compounds which are broadly defined as being protein kinase inhibitors. There are at least 400 enzymes identified as protein kinases. There is no suggestion that the compound buried in column 130 lines 53-55 would inhibit IGF-IR inhibitors, let alone a positional isomer of that compound."

First of all, whether the compound is buried in a reference or is on the cover of a scientific journal does not matter. A reference, which cites a compound of interest and which is available to public, is considered relevant. Secondly, as noted in the above rejection, a positional isomer is generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. This is all the motivation necessary to render a compound obvious. Thus, the rejection is maintained.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSANNA MOORE whose telephone number is (571)272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susanna Moore/
Examiner, Art Unit 1624

/Brenda L. Coleman/
Primary Examiner, Art Unit 1624